TB Facts

For Health Care Workers

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TUBERCULOSIS — YES! IT'S STILL A PROBLEM!

- Eight million new tuberculosis (TB) cases occur each year in the world and 3 million people die of the disease.
- In the United States, after several decades of decline, TB cases increased 20 percent between 1985 and 1992. Reasons for the increase included:
  - — The HIV epidemic
  - — Immigration of persons from areas with a high prevalence of TB
  - — Transmission of TB in high-risk environments, such as correctional facilities, homeless shelters, hospitals, and nursing homes
  - — Deterioration of the TB public health care infrastructure
- During the resurgence of TB, outbreaks of multidrug-resistant TB occurred in hospitals and prisons, resulting in high death rates and transmission to health care workers.
- The 21,337 TB cases reported in 1996 represent the fourth consecutive year of decline, suggesting the successful use of new resources in different areas of the U.S. to better detect and treat persons with active TB and latent infection.
- While the decrease in TB cases is encouraging, there are several areas of concern which will require expanded efforts:
  - — TB cases continue to increase in many areas.
  - — Outbreaks of drug-resistant TB continue in many areas.
  - — An estimated 10 to 15 million persons in the U.S. are infected with *Mycobacterium tuberculosis*. Without intervention, about 10 percent of these persons will develop TB disease at some point in life.
  - — Directly observed therapy is not available for many persons with active TB who have difficulty completing a full course of TB treatment.

— An increasing proportion of TB cases in the U.S. are among individuals born in areas with a high prevalence of TB, and international collaboration needs to be strengthened to prevent and control TB in these persons.

POPULATIONS AT RISK FOR TUBERCULOSIS

Persons at risk for TB include anyone who has ever had contact with a person with infectious TB. Some persons are considered to be at high risk for TB disease because they belong to groups in which the prevalence of TB infection is higher than it is in the general population. These groups include foreign-born persons from areas with a high prevalence of TB; residents and employees of long-term institutional settings (such as nursing homes and correctional facilities); and medically underserved populations, including the poor, the homeless, high risk racial and ethnic minority groups, and injecting drug users (IDUs). Other persons are at high risk for developing active TB disease if they become infected with *Mycobacterium tuberculosis*. They include immunocompromised persons (especially those with HIV infection), persons with other medical risk factors (such as diabetes, end-stage renal disease, and being 10 percent or more below ideal body weight), and IDUs.

HIV infection is one of the strongest known risk factors associated with the progression from TB infection to active TB disease. Studies suggest that the risk of developing TB disease is 7% to 10% each year for persons who are infected with both *M. tuberculosis* and HIV, whereas it is 10% over a lifetime for persons infected only with *M. tuberculosis*.

MODE OF TRANSMISSION

Mycobacterium tuberculosis is spread by airborne particles, known as droplet nuclei, that can be generated when persons with pulmonary or laryngeal TB sneeze, cough, speak, or sing. Persons who share the same airspace with persons with infectious TB disease are at greatest risk for infection. Infection occurs when a susceptible person inhales droplet nuclei containing tubercle bacilli and these bacilli become established in the alveoli of the lungs and spread throughout the body.

IDENTIFICATION OF PERSONS WITH TB INFECTION AND DISEASE

Identifying TB Infection

A person exposed to an individual with infectious TB or who has other risk factors for TB as noted above should be given a tuberculin skin test.

The Mantoux tuberculin skin test is the preferred method of skin testing. The Mantoux tuberculin skin test is the intradermal injection of purified protein derivative (PPD) of killed tubercle bacilli, usually on the inner forearm. The site is examined by a trained health care worker 48 to 72 hours after injection for induration (palpable swelling). The diameter of induration is measured and recorded; erythema or bruising is disregarded.

The criteria endorsed by the American Thoracic Society and CDC for a positive tuberculin skin-test result (Table 1) are intended to increase the likelihood that persons at high risk for TB will be candidates for preventive therapy and that persons having tuberculin reactions not caused by *M. tuberculosis* will not receive unnecessary diagnostic evaluation or treatment.

For each of the risk groups listed in Table 1, reactions below the cutoff point are considered negative. A negative TB skin test result does not absolutely rule out TB infection, especially in persons with TB-like symptoms, HIV infection, or AIDS. Also, because it takes 2 to 10 weeks from the time of exposure for a person to react to tuberculin, the initial skin test result of an infected contact may be falsely negative. Therefore, a repeat skin test 10 weeks post exposure is warranted.

Some persons with both HIV and TB infections may have false negative skin test reactions (anergy). **Anergy** refers to the inability to react to a skin test antigen even though the person is infected with the organism being tested. Several delayed-type hypersensitivity (DTH) antigens (such as tetanus toxoid, mumps or *Candida*) administered by the Mantoux technique have been used in an attempt to determine anergy status. Recent CDC recommendations, however, note several factors that limit the usefulness of

anergy skin testing. These include problems with standardization and reproducibility, the low risk for TB associated with a diagnosis of anergy, and the lack of apparent benefit of preventive therapy for groups of anergic HIV-infected persons. Therefore, the use of anergy testing in conjunction with PPD testing is no longer routinely recommended for screening programs for *M. tuberculosis* infection conducted among persons infected with HIV in the United States.

Persons with latent TB infection should be evaluated for HIV risk behaviors and offered counseling and HIV-antibody testing if such behaviors are present.

Many foreign countries still use **BCG** as part of their TB control programs, especially for infants. In persons vaccinated with BCG, sensitivity to tuberculin is highly variable, depending upon the strain of BCG used and the group vaccinated. There is no reliable method of distinguishing tuberculin reactions caused by BCG from those caused by natural infections. A reaction to tuberculin in a person with a history of BCG vaccination is more likely to be due to infection with *M. tuberculosis* if:

- the induration is large
- the person was vaccinated a long time ago
- the person is a recent contact of a person with infectious TB
- there is a family history of TB
- the person comes from an area where TB is common
- chest radiograph findings show evidence of previous TB

In a BCG-vaccinated person who has any of the preceding risk factors, a positive tuberculin reaction probably indicates infection with *M. tuberculosis*. Such persons should be evaluated for isoniazid preventive therapy after disease has been ruled out.

Table 1

Summary of interpretation of tuberculin skin-test results

- An induration of ≥**5 mm** is classified as positive in the following:
  - — Persons who have had recent close contact with persons who have active TB;
  - — Persons who have human immunodeficiency virus (HIV) infection or risk factors for HIV infection but unknown HIV status (e.g., injecting drug users);
  - — Persons who have fibrotic chest radiographs consistent with healed TB.
- An induration of ≥**10 mm** is classified as positive in all persons who do not meet any of the above criteria, but who belong to one or more of the following groups having high risk for TB:
  - — Injecting-drug users known to be HIV seronegative;
  - — Persons who have other medical conditions that have been reported to increase the risk for progressing from latent TB infection to active TB. These medical conditions include diabetes mellitus, conditions requiring prolonged high-dose corticosteroid therapy and other immunosuppressive therapy (including bone marrow and organ transplantation), chronic renal failure, some hematologic disorders (e.g., leukemias and lymphomas), other specific malignancies (e.g., carcinoma of the head or neck), weight loss of ≥10% below ideal body weight, silicosis, gastrectomy, jejunoileal bypass;
  - — Residents and employees of high-risk congregate settings: prisons and jails, nursing homes and other long-term facilities for the elderly, health-care facilities (including some residential mental health facilities), and homeless shelters;
  - — Foreign-born persons recently arrived (i.e., within the last 5 years) from countries having a high prevalence or incidence of TB;
  - — Some medically underserved, low-income populations, including migrant farm workers and homeless persons;
  - — High-risk racial or ethnic minority populations, as defined locally;
  - — Children <4 years of age or infants, children, and adolescents exposed to adults in high-risk categories.
- An induration of ≥**15 mm** is classified as positive in persons who do not meet any of the above criteria.

Identifying TB Disease

If the skin test result is positive or if symptoms suggestive of TB are present (e.g., productive and prolonged cough, fever, chills, loss of appetite, weight loss, fatigue, or night sweats), a chest radiograph should be obtained to help rule out active pulmonary TB. The chest radiograph may also be used to detect the presence of fibrotic lesions suggestive of old, healed TB or silicosis.

Acid-fast bacilli (AFB) smears and cultures should be performed on sputum specimens of all persons who have symptoms of TB or whose chest radiograph suggests TB. A positive AFB smear is an indication for beginning treatment for TB. However, a positive AFB smear may also indicate the presence of nontuberculous mycobacteria. A positive culture for *Mycobacterium tuberculosis* is the only definitive proof of TB disease.

Health care providers of HIV-infected persons should be aware of atypical patterns of TB disease in these persons. Extrapulmonary TB is more common. Also, pulmonary TB may present in an unusual manner (e.g., in the lymph nodes or in the lower part of the lungs).

All persons with TB infection or TB disease should be offered counseling and HIV-antibody testing, because medical management may be altered in the presence of HIV infection.

Maintain a high index of suspicion for TB in persons with undiagnosed pulmonary disease, especially in persons who are HIV seropositive.

PREVENTION OF TUBERCULOSIS

The main purpose of preventive therapy is to prevent latent infection from progressing to clinically active TB disease. Therefore, persons with positive tuberculin skin test results who do not have clinically active disease should be evaluated for preventive therapy.

Candidates for Preventive Therapy

Preventive therapy is recommended for the following persons with a positive tuberculin test result regardless of age:

- Persons with known or suspected HIV infection, including persons who inject drugs and whose HIV status is unknown (≥5mm)*
- Close contacts of persons with infectious, clinically active TB (≥5mm)*
- Persons who have chest radiograph findings suggestive of previous TB and who have received inadequate or no treatment (≥5mm)
- Persons who inject drugs and who are known to be HIV negative (≥10mm)
- Persons with certain medical conditions that have been reported to increase the risk of TB (see "Summary of interpretation of tuberculin skin-test results" on page 5) (≥10mm)

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*In some circumstances, persons in these categories may be given **preventive therapy in the absence of a positive tuberculin test result**. For example, tuberculin-negative children and adolescents who are close contacts of infectious persons and who may be infected but whose skin test result has not yet converted to positive may be given preventive therapy. If therapy is initiated, a repeat tuberculin skin test should be performed 3 months after contact has been broken with the infectious source. If the reaction is positive, therapy should be continued. If the reaction is negative, therapy may be discontinued if contact with the infectious source case continues to be broken. In addition, persons who are immunosuppressed, especially HIV-infected persons may have a negative tuberculin skin test reaction because they are anergic. All HIV-infected persons who are close contacts of persons who have infectious tuberculosis should be administered a full course of preventive therapy–regardless of tuberculin skin test results or prior courses of chemoprophylaxis–after the diagnosis of active tuberculosis has been excluded.

- Persons whose tuberculin skin test reaction converted from negative to positive within the past 2 years (≥10mm increase if younger than 35 years of age; ≥15mm increase if 35 years of age or older)

Preventive therapy is recommended for the following persons in high-incidence groups who have a positive tuberculin test result (10 or more millimeters induration), are younger than 35 years of age, and do not have additional risk factors:

- Foreign-born persons from high-prevalence areas (e.g., Latin America, Asia, and Africa)
- Medically underserved, low-income populations, including high-risk racial or ethnic groups (e.g., Asians and Pacific Islanders, blacks, Hispanics, and Native Americans)
- Residents of long-term care facilities (e.g., correctional institutions, nursing homes, and mental institutions)
- Children younger than 4 years of age
- Other groups identified locally as having an increased prevalence of TB (e.g., migrant farm workers or homeless persons)

Persons younger than 35 years of age with no known risk factors for TB should be evaluated for preventive therapy if their reaction to the tuberculin test is ≥15mm. This group should be given a lower priority for prevention efforts than the groups already listed. Tuberculin-positive staff of facilities in which a person with clinically active disease would pose a risk to large numbers of susceptible persons should also be considered for preventive therapy.

Preventive Therapy Regimens

The usual preventive therapy regimen is isoniazid (INH) (for children—10 mg/kg daily, for adults—5 mg/kg daily up to a maximum of 300 mg daily) for a minimum of 6 continuous months for adults and 6-9 continuous months for children. Twelve months is recommended for persons with HIV infection or other forms of immunosuppression. (**Note**: Persons with fibrotic infiltrates on a

chest radiograph that are thought to represent old, healed TB and those with silicosis who were formerly considered candidates for preventive therapy should receive 4 months of multidrug chemotherapy.)

To ensure that persons in high-risk groups adhere to therapy, INH can be given twice weekly at a dosage of 15 mg/kg, up to a maximum of 900 mg, using directly observed preventive therapy (DOPT). DOPT refers to the observation by a health care provider of patients as they ingest anti-TB medications.

The method of DOPT should be based on a thorough assessment of each patient's needs, living and employment conditions, and preferences. The patient and provider should agree on a method that ensures the best possible DOPT routine and that maintains the patient's confidentiality.

Situations in which patients not receiving DOPT miss appointments or demonstrate other nonadherent behavior should be brought to the attention of the appropriate public health officials. These patients should be considered for DOPT.

Persons given preventive therapy should be monitored monthly for drug side effects, especially signs and symptoms of hepatitis.

TREATMENT OF TUBERCULOSIS

Treatment Regimens

TB is usually curable if effective treatment is instituted without delay. Because of the increase in multidrug-resistant TB (MDR-TB), nearly all persons with TB should be started on a four-drug regimen of INH, rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB) or streptomycin (SM) until the drug susceptibility results are known. A less than four-drug initial regimen should only be considered if there is little possibility of drug resistance (i.e., less than 4% primary resistance to isoniazid in the community and the patient has had no previous treatment with TB drugs, is not from a country with a high prevalence of drug resistance, and has no known exposure to a patient with drug-resistant disease). If the drugs are given daily at the start of therapy and susceptibility results show no drug resistance, EMB or SM can be discontinued and the other drugs continued until PZA has been given for 2 months. INH and RIF should then be continued for another 4 months, including at least 3 months of therapy after the culture has converted to negative. Several options for daily and intermittent therapy have been published. Persons given anti-TB therapy should be monitored monthly for drug side effects.

The recommendations for the duration of TB treatment for HIV-infected persons are generally the same as for persons not infected with HIV. However, in HIV-infected patients, it is critically important to assess the clinical and bacteriologic response to therapy. Treatment should be prolonged if the response is slow or otherwise suboptimal.

Adherence

A major cause of treatment failure and drug-resistant TB is nonadherence to treatment. Treatment failure and drug-resistant TB threaten the health of TB patients. These factors also pose serious public health risks because they can lead to prolonged infectiousness and the transmission of TB within the community.

One way to ensure that patients adhere to therapy is to use directly observed therapy (DOT). DOT means that a health care worker or another designated person watches the patient swallow each dose of TB medication. DOT should be considered for all patients because clinicians are often inaccurate in predicting which patients will adhere to medication on their own.

In many areas, patients are routinely given DOT. DOT has been shown to be cost-effective when intermittent regimens are used. Nearly all the treatment regimens for drug-susceptible TB can be given intermittently if they are directly observed; using intermittent regimens reduces the total number of doses a patient must take, as well as the total number of encounters with the health care provider or outreach worker. Furthermore, DOT can significantly reduce the frequency of acquired drug resistance and relapse.

Other measures commonly used to promote adherence include:

- Developing an individualized treatment plan for each patient
- Working with outreach staff from the same cultural and linguistic background as the patient
- Educating the patient about TB medication dosage and possible adverse reactions
- Using incentives and enablers to remove barriers to adherence (e.g., transportation tokens and food vouchers)
- Facilitating access to health and social services

REPORTING

TB reporting is required by law in every state. All new TB cases and suspect cases should be reported promptly to the health department by the clinician. Cases may also be reported by infection control nurses or by pharmacies when TB drugs are dispensed. In addition, all positive TB smears and cultures should be reported promptly by laboratories. Early reporting is important for the control of TB and it gives clinicians access to the resources of the health department for assistance in case management (e.g., DOT) and contact investigation.

MULTIDRUG-RESISTANT TUBERCULOSIS (MDR-TB)

An extremely serious aspect of the TB problem in the United States is MDR-TB (i.e., TB resistant to at least isoniazid and rifampin). **MDR-TB can usually be prevented by initially treating TB patients with four drugs and by administering TB medications on a directly observed basis**. Persons at high risk for MDR-TB include persons who have been recently exposed to MDR-TB, especially if they are immunocompromised; TB patients who failed to take medications as prescribed; TB patients who were prescribed an ineffective treatment regimen; and persons previously treated for TB.

MDR-TB presents difficult treatment problems. Treatment must be individualized and based on the patient's medication history and drug susceptibility study results. **Clinicians who are not familiar with the management of patients with MDR-TB disease or with patients infected with multidrug-resistant organisms should seek expert consultation.**

For persons likely to have been infected with *M. tuberculosis* resistant to both isoniazid and rifampin, observation without preventive therapy is usually recommended because only isoniazid and rifampin have been evaluated for preventive therapy. However, for persons at an especially high risk for TB disease once infected (e.g., persons with HIV infection), preventive therapy with an alternative regimen should be strongly considered.

INFECTION CONTROL MEASURES

The spread of TB in health care settings can be minimized by implementing CDC recommendations for preventing TB transmission in these settings. The early detection, isolation, and treatment of disease in persons with infectious TB are essential to controlling transmission. TB should be suspected in all persons with symptoms consistent with TB (for example, cough, fever, night sweats, chills, fatigue, weight loss or loss of appetite), especially those with confirmed or suspected HIV infection and undiagnosed pulmonary disease. Precautions should be taken to prevent airborne transmission of infection until TB is diagnosed and treated or ruled out.

Effective AFB isolation should be initiated for persons with confirmed or suspected TB to reduce the risk that they will expose others. Precautions should be taken during and immediately after procedures that may induce coughing, such as bronchoscopy, sputum collection, the aerosol induction of sputum, and the administration of aerosolized medication, such as pentamidine.

Antituberculosis drug treatment should be promptly initiated for persons with active disease to render them noninfectious. Persons at high risk for TB infection should be screened and, if infected, evaluated for preventive therapy. Ongoing TB screening should be provided to health care workers who have regular contact with persons with TB or HIV infection.

Remember! The key to preventing TB infection and death and disability from TB disease is to consider the possibility of TB in high-risk groups, make the diagnosis as quickly as possible, and initiate effective, directly observed drug therapy for persons found to have TB. Think TB!

FOR ADDITIONAL INFORMATION, CONTACT YOUR LOCAL HEALTH DEPARTMENT

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